

[0042] Another aspect of the present invention is directed a method of producing an electrospray device including providing a substrate having opposed first and second surfaces, at least the first side is coated with a photoresist over an etch-resistant material. The photoresist on the first surface is exposed to an image to form a pattern in the form of at least one ring on the first surface. The exposed photoresist is removed on the first surface which is outside and inside the at least one ring leaving the unexposed photoresist. The etch-resistant material is removed from the first surface of the substrate where the exposed photoresist was removed to form holes in the etch-resistant material. Photoresist is removed from the first surface. Photoresist is provided over an etch-resistant material on the second surface and exposed to an image to form a pattern circumscribing extensions of the at least one ring formed in the etch-resistant material of the first surface. The exposed photoresist on the second surface is removed. The etch-resistant material on the second surface is removed coincident with where the photoresist was removed. Material is removed from the substrate coincident with where the etch-resistant material on the second surface was removed to form a reservoir extending into the substrate. The remaining photoresist on the second surface is removed. The second surface is coated with an etch-resistant material. The first surface is coated with a second coating of photoresist. The second coating of photoresist within the at least one ring is exposed to an image. The exposed second coating of photoresist is removed from within the at least one ring to form at least one hole. Material is removed from the substrate coincident with the at least one hole in the second layer of photoresist on the first surface to form at least one passage extending through the second layer of photoresist on the first surface and into substrate to the extent needed to reach the etch-resistant material coating the reservoir. Photoresist from at least the first surface is removed. An etch-resistant layer is applied to all exposed surfaces of the substrate. Material is removed from the substrate exposed by the removed etch-resistant layer around the at least one ring to define at least one nozzle on the first surface. The etch-resistant material coating the reservoir is removed from the substrate. An etch resistant material is applied to coat all exposed surfaces of the substrate. At least one of the reservoir and the at least one passage is filled with a polymerizable material. The polymerizable material is then polymerized.

[0043] Another aspect of the present invention relates to a method of producing an electrospray device. An electrospray device is provided having an injection surface having an entrance orifice and a reservoir in fluid communication with the entrance orifice. An ejection surface opposes the injection surface and has an exit orifice. A channel extends through the substrate between the entrance orifice and the exit orifice. A recess extends into the ejection surface and surrounds the exit orifice. An electric field generating source is positioned to define an electric field which surrounds the exit orifice. At least one of the passage and the reservoir is filled with a polymerizable material and polymerized.

[0044] Another aspect of the present invention relates to a separation block. The separation block includes an injection surface having a plurality of entrance orifices. An ejection surface opposes the injection surface and has a plurality of exit orifices each corresponding to a respective one of the plurality of entrance orifices. A plurality of channels extends through the substrate between one of the plurality of

entrance orifices and the corresponding one of the plurality of exit orifices. The channels are filled with a separation material suitable to effect chromatographic separation of analytes passing through the block.

[0045] Another aspect of the present invention relates to a separation block system including a plurality of separation blocks described above, wherein the separation blocks are stacked one upon the other and each of the plurality of exit orifices of one block are aligned with the corresponding one of the plurality of entrance orifices of the other block.

[0046] Another aspect of the present invention relates to a method for processing samples of fluid including passing at least one sample through a respective one of a first array of multiple through-substrate channels containing a first separation material suitable to effect chromatographic separation of analytes passing through. The at least one sample is passed from the first array through a respective one of a second array of multiple through-substrate channels containing a second separation material having the same or different separation characteristics than the first separation material. Optionally, the previous step is repeated sequentially with one or a plurality of arrays of multiple through-substrate channels. The at least one sample is passed to corresponding entrance orifices of a system of electrospray devices. The at least one sample is electrosprayed and passed to a detector, which detects at least one analyte in the electrospray. The electrospray can be detected by sequentially spraying each electrospray in communication with the detector. The electrospray can also be detected by simultaneously spraying a plurality of electrosprays and sweeping the detector in communication with the electrosprays.

[0047] The present invention relates to the complete integration of microchip-based separations and electrospray ionization within a single microfabricated device. A continuous or monolithic polymer bed formed by in situ polymerization of a monomer solution containing a porogen can be contained within the separation channel in this integrated device. The present invention is directed toward improving coupling of microchip-based separations and electrospray mass spectrometry. This present invention discloses the integration of a polymer monolith within a separation channel formed through a silicon monolith together with an electrospray nozzle microfabricated using Micro-Electro-Mechanical Systems technology. The integration of a microchip-based polymer monolithic column and electrospray is a significant advance over prior disclosed systems and methods.

[0048] The electrospray device of the present invention can generate multiple electrospray plumes from a single fluid stream and be simultaneously combined with mass spectrometry. Each electrospray plume generates a signal for an analyte contained within a fluid that is proportional to that analytes concentration. When multiple electrospray plumes are generated from one nozzle, the ion intensity for a given analyte will increase with the number of electrospray plumes emanating from that nozzle as measured by the mass spectrometer. When multiple nozzle arrays generate one or more electrospray plumes, the ion intensity will increase with the number of nozzles times the number of electrospray plumes emanating from the nozzle arrays.

[0049] The present invention achieves a significant advantage in terms of high-sensitivity analysis of analytes by